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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,919	12/12/2003	Kathleen Gilbert	D6199D2	2261

7590 06/10/2005

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EXAMINER

SHIAO, REI TSANG

ART UNIT	PAPER NUMBER
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1626

DATE MAILED: 06/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/734,919

Applicant(s)

GILBERT ET AL.

Examiner

Robert Shiao

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on responses filed on 12/06/2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-29 and 41 is/are pending in the application.
- 4a) Of the above claim(s) 41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. This application claims benefit of the provisional application: 60/136,579 with a filing date 05/28/1999.
2. Amendment of claims 23, 25-29, and cancellation of claims 1-22, and 30-40 in the amendment filed on December 06, 2004, is acknowledged. Claims 23-29 and 41 are pending in the application.

Responses to Election/Restriction

3. Applicant's election without traverse of Group VI claims 23-29 in the reply filed on December 06, 2004, is acknowledged.

Status of the Claims

4. Claims 23-29 and 41 are pending in the application. The scope of the invention of the elected subject matter is as follows:

Claims 23-29, in part, drawn to methods of use (i.e., inactivating antigen-specific T cells) using compounds of formula (II), wherein the variable Y represents O thereof. Claims 23-29, in part, embraced in above elected subject matter, are prosecuted in the case. Claims 23-29, in part, not embraced in above elected subject matter, and claim 41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The requirement is still deemed proper and is therefore made **FINAL**.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter "inactivating antigen-specific cells", "prophylaxis", or "a disorder involving an autoimmune component or a neoplastic disease" without limitation, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, see claims 23 or 26, lines 1-5.

6. Claim 23-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the instant methods treating rheumatoid arthritis, does not reasonably provide enablement for a method of preventing (i.e., prophylaxis) inactivating antigen-specific T cells, i.e., diseases other than autoimmune diseases or renal cancer. The specification does not enable any person skilled in the art to which it pertains, with which it is most nearly connected, to use the invention commensurate in scope with these claims, see claims 23 or 26, lines 1-5.

For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1988):

- 1) Nature of invention.
- 2) State of prior art.

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- 3) Level of ordinary skill in the art.
- 4) Level of predictability in the art.
- 5) Amount of direction and guidance provided by the inventor.
- 6) Existence of working examples.
- 7) Breadth of claims.
- 8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See below:

1) Nature of the invention

The claims are drawn to methods of use using compounds of the formula in claim 23 without limitation of "inactivating antigen-specific cells", "prophylaxis", or "a disorder involving an autoimmune component or a neoplastic disease".

2) State of the prior art

The reference Bekkali et al. US 6,313,117 does not indicate which compounds of instant compounds may be useful in the claimed invention. Bekkali et al. '117 is pertaining to Preparation of succinic acid diamides as cysteine protease inhibitors.

3) Level of ordinary skill in the art.

The level of ordinary skill in the art is high. The claims are drawn to methods of use using compounds of the formula in claim 23 without limitation of "inactivating antigen-specific cells", "prophylaxis", or "a disorder involving an autoimmune component or a neoplastic disease" by the instant examples disclosed in the specification.

4) Level of predictability in the art.

The claims are drawn to methods of use using compounds of the formula in claim 23 without limitation of "inactivating antigen-specific cells", "prophylaxis", or "a disorder involving an autoimmune component or a neoplastic disease", there would be little predictability in the scope of claimed methods.

5) Amount of direction and guidance provided by the inventor.

The claims are drawn to methods of use using compounds of the formula in claim 23 without limitation of "inactivating antigen-specific cells", "prophylaxis", or "a disorder involving an autoimmune component or a neoplastic disease", which are neither enabled nor supported in the specification.

6) Existence of working examples.

The claims are drawn to methods of use using compounds of the formula in claim 23 without limitation of "inactivating antigen-specific cells", "prophylaxis", or "a disorder involving an autoimmune component or a neoplastic disease", however, the specification provides only limited examples of methods.

7) Breadth of claims.

The claims are extremely broad due to the vast number of possible "methods of use using compounds of the formula in claim 23 without limitation of "inactivating antigen-specific cells", "prophylaxis", or "a disorder involving an autoimmune component or a neoplastic disease"".

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification did not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with this claim. In particular, the specification failed to enable the skilled artisan to practice the invention without undue experimentation. The skilled artisan would have a numerous methods in order to obtain "methods of use using compounds of the formula in claim 23 without limitation of "inactivating antigen-specific cells", "prophylaxis", or "a disorder involving an autoimmune component or a neoplastic disease"" as claimed. Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims, one skilled in the art could not perform the claimed compounds without undue experimentation, see *In re Armbruster* 185 USPQ 152 CCPA 1975. Incorporation of the limitation "methods of use using compounds of the formula in claim 23 without limitation of "inactivating antigen-specific cells", or "a disorder involving an autoimmune component or a neoplastic disease"", i.e., diseases of claims 27-29, etc., and elimination of the limitation "prophylaxis", would obviate the rejection, see pages 13-14.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

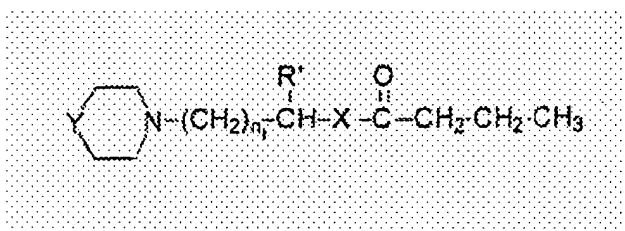
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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23-29 are rejected under 35 U.S.C. 102(b) as being anticipated by

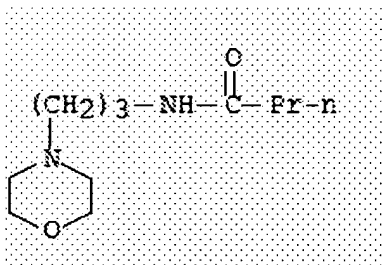
(1) Kotelko et al., publication, *Acta Poloniae Pharmaceutica* (1973), 30(2), 135-43, see CAS: 79:105217; or (2) Kadlubowski's publication, *Wiadomosci Parazytologiczne* (1978), 24(5), 575-9, see CAS: 90:197759.

Applicants claim a method of use using compounds of the formula,



, wherein the variable X represents O or NH; the variable Y represent O; and the variable R' represents hydrogen, methyl or ethyl; the variable n1 represents an integer from 1 to 5, and the instant compounds and methods of use have been found on the pages 4-51 of the specification.

Kotelko et al. disclose a compound Butanamide, N-[3-(4-morpholinyl)propyl]- ,

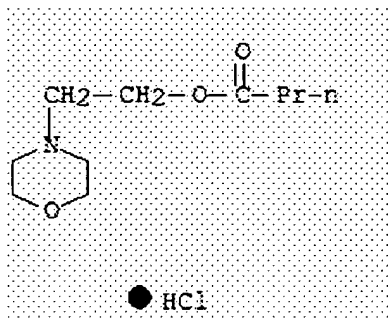


, clearly anticipate the instant compounds of the formula of claim 23, wherein the variable X represent NH; the variable Y represents O; the variable R' represents hydrogen; the variable n1 is 2, see RN: 49808-41-5 of DN: 79:105217.

Kadlubowski discloses a compound Butanoic acid, 2-(4-morpholinyl)ethyl ester,

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hydrochloride,



, clearly anticipate the instant compounds or its salt of the formula of claim 23, wherein the variable X represents O; the variable Y represents O; the variable R' represents hydrogen; the variable n1 is 1, see RN: 23866-07-1 of DN: 90:197759.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating

obviousness or nonobviousness.

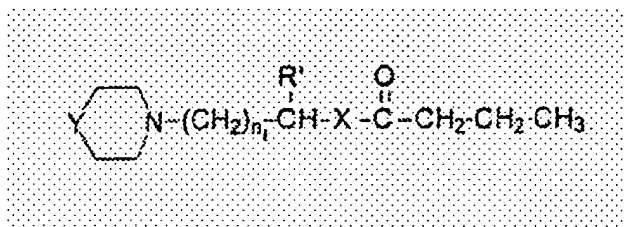
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

"Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Also see M.P.E.P. 2113.

9. Claims 23-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kotelko et al., publication, Acta Poloniae Pharmaceutica (1973), 30(2), 135-43, see CAS: 79:105217;

Applicants claim a method of use (i.e., treating diseases) using compounds of the formula,

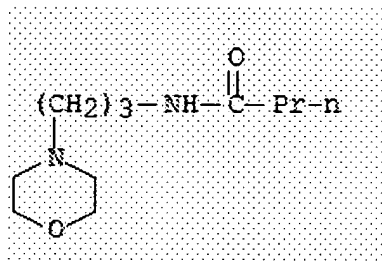
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, wherein the variable X represents O or NH; the variable Y represent O; and the variable R' represents hydrogen, methyl or ethyl; the variable n1 represents an integer from 1 to 5, and the instant compounds and methods of use have been found on the pages 4-51 of the specification.

Determination of the scope and content of the prior art (MPEP §2141.01)

Kotelko et al. disclose a compound Butanamide, N-[3-(4-morpholinyl)propyl]- ,

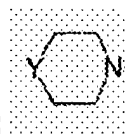


, as pharmacological agents (i.e., treating diseases), see

DN: 79:105217.

Determination of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and Kotelko et al. is that the



instant carbon chain number between variable X and moiety is having from two to six carbon atoms, while Kotelko et al. have three carbon atoms at the same

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position.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the claims 23-29 prima facie obvious because one would be motivated to employ the compound of Kotelko et al. to obtain instant methods of use, wherein the variable X represent NH; the variable Y represents O; the variable R' represents hydrogen or methyl; the variable n1 is 1-5.

However, H and alkyl (methyl) are art recognized equivalents. *In re Lincoln*, 126 USPQ 477, 53 USPQ 40 (CCPA, 1942); *In re Druey*, 319 F.2d 237, 138 USPQ 39 (CCPA, 1963); *In re Lohr*, 317 F.2d 388, 137 USPQ 548 (CCPA, 1963); *In re Hoehsema*, 399 F.2d 269, 158 USPQ 598 (CCPA, 1968); *In re Wood*, 582 F.2d 638, 199 USPQ 137 (CCPA, 1978); *In re Hoke*, 560 F.2d 436, 195 USPQ 148 (CCPA, 1977); *Ex parte Fauque*, 121 USPQ 425 (POBA, 1954); *Ex parte Henkel*, 130 USPQ 474, (POBA, 1960).

Applicant is reminded that when the difference between Kotelko et al. compounds is only in the length of a carbon chain (e.g. methyl, ethyl, propyl, etc.) are adjacent homologs. However, adjacent homologs are prima facie obvious. *In re Henze*, 85 USPQ 261 (1950). Therefore, the instant invention is prima facie obvious over Kotelko et al.

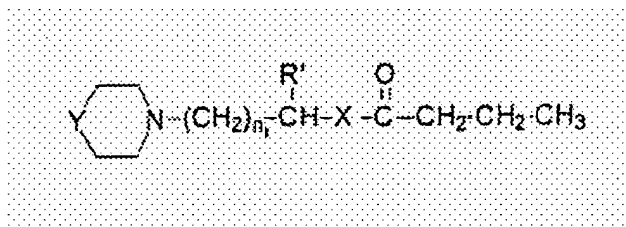
The motivation to make the claimed compounds derives from the expectation that the instant claimed compounds would possess similar activities, i.e., pharmacological agents for treating diseases, from the known Kotelko et al. compounds to that

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which is claimed in the reference.

10. Claims 23-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kadlubowski's publication, Wiadomosci Parazytologiczne (1978), 24(5), 575-9, see CAS: 90:197759.

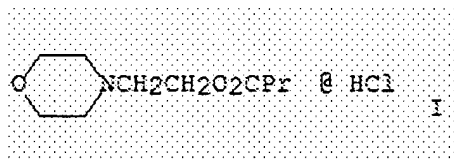
Applicants claim a method of use (i.e., treating diseases) using compounds of the formula,



, wherein the variable X represents O or NH; the variable Y represent O; and the variable R' represents hydrogen, methyl or ethyl; the variable n1 represents an integer from 1 to 5, and the instant compounds and methods of use have been found on the pages 4-51 of the specification.

Determination of the scope and content of the prior art (MPEP §2141.01)

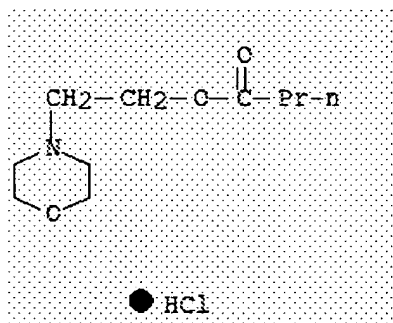
Kadlubowski discloses a compound of the formula (I),



, as pharmacological active compounds, i.e., treating

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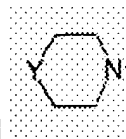
diseases. A number of compounds have been specifically exemplified, i.e., Butanoic acid, 2-(4-morpholinyl)ethyl ester, hydrochloride of the formula,



, see DN:90 197759.

Determination of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and Kadlubowski's is that the



instant carbon chain number between variable X and moiety is having from two to six carbon atoms, while Kadlubowski's have two carbon atoms at the same position.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the claims 23-29 prima facie obvious because one would be motivated to employ the compound of Kadlubowski's to obtain instant methods of use, wherein the variable X represent O; the variable Y represents O; the variable R' represents hydrogen or methyl; the variable n1 is 1-5.

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However, H and alkyl (methyl) are art recognized equivalents. *In re Lincoln*, 126 USPQ 477, 53 USPQ 40 (CCPA, 1942); *In re Druey*, 319 F.2d 237, 138 USPQ 39 (CCPA, 1963); *In re Lohr*, 317 F.2d 388, 137 USPQ 548 (CCPA, 1963); *In re Hoehsema*, 399 F.2d 269, 158 USPQ 598 (CCPA, 1968); *In re Wood*, 582 F.2d 638, 199 USPQ 137 (CCPA, 1978); *In re Hoke*, 560 F.2d 436, 195 USPQ 148 (CCPA, 1977); *Ex parte Fauque*, 121 USPQ 425 (POBA, 1954); *Ex parte Henkel*, 130 USPQ 474, (POBA, 1960).

Applicant is reminded that when the difference between Kadlubowski's compounds is only in the length of a carbon chain (e.g. methyl, ethyl, propyl, etc.) are adjacent homologs. However, adjacent homologs are prima facie obvious. *In re Henze*, 85 USPQ 261 (1950). Therefore, the instant invention is prima facie obvious over Kotelko et al.

The motivation to make the claimed compounds derives from the expectation that the instant claimed compounds would possess similar activities, i.e., pharmacological agents for treating diseases, from the known Kadlubowski's compounds to that which is claimed in the reference.

Objection

11. Claim 41 is objected to as being a non-elected invention. Elimination of claim 41 would obviate the objection.

Telephone Inquiry


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


TAOFIQ SOLOLA
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Robert Shiao, Ph.D.
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June 06, 2005